ECZEMA VACCINATUM: REPORT OF TWO CASES WITH A REVIEW OF THE LITERATURE[1]

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There is much confusion in the literature concerning proper titles for various vaccinial eruptions which give similar clinical pictures and much disagreement as to etiologic agents. In 1887 Kaposi (1) described a rare vaccinial type of eruption that occurred as a complication of infantile eczema. Two years later Juliusberg (2) described what is now thought to be the same disease, calling it pustulosis vacciniformis acuta thinking it was caused by a pyogenic staphylococcus. Generalized vaccinia, according to Danziger (3), was first studied and classified in 1881 by Behrerd. Since that time, there has been a voluminous accumulation of literature concerning generalized vaccinial-like eruptions.

Ellis (4) in 1935 reviewed the literature discussing the impossibility of the differentiation of eczema vaccinatum, Kaposi's varicelliform eruption, and pustulosis vacciniformis acuta. He stated that it was impossible to tell these diseases apart clinically and that diagnosis could be made only by identification of the vaccinia virus, or by a corneal inoculation test. Ellis also expressed the opinion that eczema vaccinatum and generalized vaccinia were essentially the same process and the virus in both instances was disseminated by the blood stream. McLachlin and Gillespie (5) in 1936 studied an epidemic of 16 cases without determining an etiological agent. No virus studies were attempted. Their chief suspect was one of the streptococcus group. Bettley (6) in 1937 reported one case in which he was unable to identify a virus. He used the Paul test which elicited a negative reaction and concluded this was not a virus infection. Many others, Strickler (7), Corson and Lundy (8), McLachlin (9), Pepple, Murrell, and Fowlkes (10), Goeckerman and Wilhelm (11), and Brain and Lewis (12). Tedder (13) (1936) and Ronchese (14) (1943) felt that all the vaccinial eruptions were the same disease and possessed a common etiological agent.

King (15) (1939) reported five cases, one of which began as a herpes zoster. Wise and Sulzberger (16) suggested that Kaposi's varicelliform eruption might very well be a separate disease from eczema vaccinatum and suggested the possibility of its being caused by inoculation or hematogenous distribution of the herpes virus. Barton and Brunsting (17) in 1943 did not determine an etiological agent for the clinical picture presented in their case although they suggested the possibility of a virus etiology. The following year they (18) described the results of an experimental study in two cases of Kaposi's varicelliform eruption in which the virus isolated from the patients was shown to be that of herpes simplex. No evidence of the presence of vaccinia virus was obtained. They called attention

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to the work by Seidenberg in Germany who demonstrated a definite etiologic relation of herpes virus to Kaposi's varicelliform eruption. In this same year several other reports and studies were made.

Wedder (19) in 1944 made a study of the complications of infantile eczema caused by the virus of herpes simplex. He gave an excellent discussion and description of its clinical characteristics. He felt the herpes simplex virus was the cause of Kaposi's varicelliform eruption thus distinguishing it from generalized vaccinia caused by the vaccinia virus. Lane and Herold (20) in 1944 reported five cases in which they opposed previous investigators' consideration that eczema vaccinatum, generalized vaccinia pustular acuta variformis, and Kaposi's varicelliform eruption were the same and should be called dermatitis vaccinia. They believed that Kaposi's varicelliform eruption was a unique and separate disease caused by a virus, probably a strain of the virus of herpes simplex. Lynch (21) in 1945 reported two cases and expressed the opinion that eczema vaccinatum was a distinct entity caused by the virus of vaccinia, and that Kaposi's and Juliusberg's terms applied to a group of disorders resulting from the virus of herpes simplex. Lynch's experimental studies confirmed the results of other workers in identifying the herpes virus. Lynch (22) has subsequently reported four additional cases of Kaposi's varicelliform eruption and states that Esser (23) and Seidenberg (24) in 1941 first contributed evidence that the virus of the herpes simplex caused Kaposi's varicelliform eruption in some instances. Barton and Brunsting (18) called attention to this German work in 1944. Most all of the American studies were apparently done without knowledge of Esser and Seidenberg's discovery.

This group of diseases presents a similar clinical picture, but, there are certain differences which are sufficient to suggest the diagnosis without laboratory procedures. In eczema vaccinatum there is usually a history of a vaccinia contact; and frequently in Kaposi's varicelliform eruption, there is a history of contact or previous eruption of herpes simplex. Both diseases are usually seen in children with infantile eczema. These diseases are usually acute with a febrile course. There have been some reported cases terminating fatally, but the usual course is for recovery with symptomatic treatment. The lesions in generalized vaccinia go through the typical stages of a vaccinia eruption. The lesions may coalesce and produce a large bullous lesion, or they may undergo involution through the stages of desiccation, crust formation and final exfoliation. Commonly there is much edema and swelling of the face with a regional adenitis. There may be a close clinical resemblance of Kaposi's varicelliform eruption to generalized vaccinia. The resemblance in some cases may be slight, as the vesicles in Kaposi's varicelliform eruption are often typically herpetic. The inflammatory papules quickly become vesicular, are tense, umbilicated, and soon rupture. The lesions situated on an inflammatory base are subject to trauma and secondary infection. Frequently, the grouping of the lesions, characteristic of herpes simplex, is striking. The diagnosis is established by virus studies. Points of importance in a differential diagnosis are shown in figure 1.

REPORT OF CASES

Case 1. W. P. W. The patient, a five year old negro boy, was seen with a chief complaint of a generalized pustular eruption of two days' duration on the site of a previous eczema. Since birth, the patient had had periods of infantile eczema. Three weeks before the onset of the presenting illness, the patient's older sister was vaccinated at school. The patient slept in the same bed with the vaccinated sister. Eighteen days after the sister's vaccination (from which she obtained a "take"), the patient's parents noticed a pustular eruption over the patient's face and thighs. This eruption spread and at the time of the admission, the child had developed fever, chills and was acutely ill.

The patient had never been vaccinated and had not been previously exposed to a person vaccinated. Since birth, he had had infantile eczema with recurrent periods of remissions and exacerbations. The patient had had three asthmatic attacks during the past year.

The face, neck, extensor surfaces of the thighs and calves were covered with numerous discrete pustular lesions showing umbilication. There was marked edema and distortion

FIG. 1. DIFFERENTIAL DIAGNOSIS

	ECZEMA VACCINATUM	KAPOSI'S VARICELLIFORM ERUPTION
Recent smallpox vaccination or contact with recent vaccination	Yes	No
Recent herpes simplex or contact with herpes simplex	No	Yes
Age	Children	Adults
Type of lesion	Papules, umbilicated pustules	Herpetic grouped vesicles
Paul's Test	Negative	Positive
Herpetic inclusion bodies in cornea of rabbit	No	Yes
Guarnieri bodies and Paschen bodies in cornea of rabbit	Yes	No
Immune bodies-precipitation test specific for:		
Virus of herpes simplex	No	Yes
Virus of vaccinia	Yes	No

of the face, the right eye being entirely closed (fig. 2). The eyes were normal except for the edema and the cutaneous lesions on the lids. There was a generalized adenitis. The remainder of the physical examination was essentially negative.

Microscopic examination of the skin revealed an extensive necrosis of the epidermis with an infiltration of polymorphonuclear cells and round cells. The lower layers of the epidermis were involved as well as the corium. The picture was one of a necrotic ulcerative lesion which had advanced beyond the stage of vesicular and pustular formation.

Virus studies were done. The scarified skin of a rabbit was inoculated with crusts and serum. On the 11th day, a definite pustular lesion had developed. The scarified cornea was inoculated with the same material. Guarnieri bodies and Paschen's granules were not seen. A Giemsa stained smear, however, showed what appeared to be elementary bodies. Vaccinial material and anti-vaccinia rabbit serum showed slight floccular precipitates on the 5th day. Other accessory clinical findings were essentially normal.

Warm saline compresses were started on admission and 10,000 units of penicillin were given intramuscularly every three hours. After seven days, the temperature reached and maintained a normal level. The generalized adenitis had decreased. The skin lesions had

receded and desquamated. The edema had completely disappeared. Clean granulation tissue was present. At this time, the saline compresses were discontinued and simple boric acid ointment was applied to all lesions. The patient was discharged twenty-two days after admission. All the lesions completely epithelized.

Case 2. W. S. The patient, a nine month old negro infant, was admitted to the hospital with a chief complaint of a generalized eruption. The patient had had erythematous, scal-

FIG. 2.

ing, weeping, oozing infantile eczema since birth. Thirteen days prior to admission, the patient's older sister was vaccinated for small-pox at a local school. She returned home immediately after vaccination and nursed the patient the remainder of that day. Ten days later, the patient developed a vesicular eruption over his face and hands at the site of the infantile eczema. At this time, the patient was seen by a dermatologist who made a diagnosis of Kaposi's varicelliform eruption. The patient developed high fever, chills, and became lethargic.

The patient was a thin, acutely ill infant. The entire face, head and arms were covered

with a diffuse vesicular, pustular eruption. There was much weeping and crusting; numerous unruptured pustules showed umbilication. There were a few discrete, scattered vesicular and pustular lesions over the chest and arms. There was marked edema and swelling of the face and eyelids so that the eyes were closed. The eye, cornea and conjunctiva were normal. There was generalized adenitis. The cervical chain was markedly enlarged and tender (fig. 3).

The histopathological picture of a typical lesion removed from the leg showed a picture

FIG. 3.

of vaccinia. With a Giemsa stain, border epithelial cells showed large inclusion bodies as well as small inclusion bodies.

The following virus studies were done. The scarified skin of a rabbit was inoculated with crusts, serum and pus. A vesicle appeared within ten days and by the fifteenth day formed a pustule. No Guarnieri bodies or Paschen's granules were observed in the material obtained from the rabbit's cornea. Vaccinial material and anti-vaccinial rabbit serum showed a slight floccular precipitate. The Paul test, as performed two days after admission, was negative on 24, 48 and 72 hour readings.

On admission, the patient's temperature was 39.8°C. The patient was given aqueous

penicillin 10,000 units intramuscularly every three hours and normal saline compresses were applied to all lesions. Phenobarbital sedation and accessory vitamins were given. Within 48 hours, the temperature returned to normal and remained so. The lesions slowly regressed and twelve days after admission were markedly improved. Edema of the eyes had receded, temperature had remained normal, and the penicillin was discontinued. Three days later, the patient developed broncho-pneumonia and became febrile. Penicillin was again started and within four days the pneumonia had resolved. The temperature became normal and the skin lesions continued to improve. Saline compresses were discontinued and the patient received only a simple boric acid ointment twice daily. One 3 centimeter area over the occipital region became infected and within a few days a slough left a 2 centimeter gaping area in the scalp. Saline compresses were applied to the lesion which slowly granulated and became epithelized. The patient was discharged sixty-three days after admission with the skin well healed and scarless.

SUMMARY

1. The recent literature has been reviewed in an effort to disassociate Kaposi's varicelliform eruption and eczema vaccinatum.

2. As a result of experimental studies in this country and abroad it appears that the herpes simplex virus, or a virus closely related to it, may be responsible for Kaposi's varicelliform eruption.

3. From a review of this literature, it would appear that generalized vaccinia and Kaposi's varicelliform eruption can be differentiated clinically.

4. Two patients with generalized vaccinia in whom virus studies were made are reported.

BIBLIOGRAPHY

1. Kaposi, M. J.: Pathologie and Therapie der Hautkrarkheiter. Berlin, Urbar & Schwarzenberg 1887, p . 483.
2. Juliusberg, F.: Veber Pustulosis Acuta Varioliformis. Arch. Dermat. & Syph., **46** 21, 1898.
3. Danziger, Felix: Veber Vaccine Generalisata. München. med. Wchnschr., **54:** 1583 1907.
4. Ellis, Francis: Eczema vaccinatum: its relation to generalized vaccinia. J. A. M. A., **104:** 1891–1894, 1935.
5. McLachlin, A. D., and Gillespie, M.: Kaposi's varicelliform eruption: an epidemic of 16 cases. Brit. J. Dermat., **48:** 337, 1936.
6. Bettley, F. R.: Kaposi's varicelliform eruption: some extensive findings. Brit. J. Dermat., **52:** 222, 1937.
7. Strickler, Albert: Kaposi's varicelliform eruption: a report of five cases. Urol. & Cutan. Rev., **48:** 340, 1944.
8. Corson, E. F., and Lundy, J. B.: Kaposi's varicelliform eruption: report of three cases. Am. J. Dis. Child., **50:** 1436–1481, 1935.
9. McLachlin, A. D.: Kaposi's varicelliform eruption. Brit. J. Dermat., **46:** 8, 1934.
10. Pepple, A. W., Muerell, J. W., and Fowlkes, R. W.: Varicelliform eruption of Kaposi. South. M. J., **35:** 667, 1942.
11. Goeckerman, W. H., and Wilhelm, L. F.: Kaposi's varicelliform eruption: report of a case. Arch. Dermat. & Syph., **32:** 59–61, 1935.
12. Brain, R. T., and Lewis, B.: Investigation of virus diseases of skin, with report of case of Kaposi's varicelliform eruption. Brit. J. Dermat., **49:** 551, 1937.
13. Tedder, J. W.: Eczema vaccinatum. Arch. Dermat. & Syph., **34:** 1008–1023, 1936.
14. Ronchese, F.: Kaposi's varicelliform eruption: dermatitis vaccinia. Arch. Dermat. & Syph., **47:** 613, 1943.

15. KING, A. D.: Kaposi's varicelliform eruption. Arch. Dermat. & Syph., **39:** 1035–1039, 1939.
16. Year Book of Dermatology & Syphilology 1942, pg. 151–152.
17. BARTON, R. L., AND BRUNSTING, L. A.: Kaposi's varicelliform eruption: report of a case. Proc. Staff Meeting, Mayo Clinic, **18:** 199, 1943.
18. BARTON, R. L., AND BRUNSTING, L. A.: Kaposi's varicelliform eruption. Arch. Dermat. & Syph., **50:** 99, 1944.
19. WEDDER, H. A.: Complication of infantile eczema carried by the virus of herpes simplex. Am. J. Dis. Child., **67:** 247, 1944.
20. LANE, C. W., AND HEROLD, W. C.: Kaposi's varicelliform eruption: report of five cases. Arch. Dermat. & Syph., **50:** 396, 1944.
21. LYNCH, FRANCIS: Kaposi's varicelliform eruption. Arch. Dermat. & Syph., **51:** 129, 1945.
22. LYNCH, F. W., AND STEVENS, R. J.: Kaposi's varicelliform eruption. Arch. Dermat. & Syph., **55:** 327, 1947.
23. ESSER, M.: Ueber eine kleine Epidemie von Pustulosis varioliformis acuta. Ann. paediat., **157:** 156, 1941.
24. SEIDENBERG, S.: Zur Aetiologie der Pustulosis vacciniformis acuta. Schweiz. Ztschr. f. Path. u. Bakt., **4:** 398, 1941.